Overexpression of HexA/HexB by lentivector expression in blood cells to treat Tay-Sachs and Sandhoff disease

Grant Award Details

Overexpression of HexA/HexB by lentivector expression in blood cells to treat Tay-Sachs and Sandhoff disease

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-08519

Project Objective: Our objective is to have a pre-IND meeting

Investigator:

Name:	Joseph Anderson
Institution:	University of California, Davis
Type:	PI

Disease Focus: Metabolic Disorders, Neurological Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $883,174

Status: Active

Progress Reports

Reporting Period: OM#1

View Report

Grant Application Details

Application Title: Overexpression of HexA/HexB by lentivector expression in blood cells to treat Tay-Sachs and Sandhoff disease

Public Abstract:

Translational Candidate

Autologous hematopoietic stem cells transduced with a lentiviral vector expressing wild type human HexA and HexB.

Area of Impact

The therapeutic candidate would halt disease progression in Tay-Sachs and Sandhoff disease patients who have no curative or ameliorating treatment.

Mechanism of Action

Wild type HexA and HexB will be delivered to affected neurons through cross correction by immune cells derived from lentivector transduced hematopoietic stem cells. This will result in a renewed degradation of accumulated GM2-gangliosides thus rescuing affected neurons and halting disease progression. The combination of gene therapy and hematopoietic stem cells offers a promising approach for constitutive and life-long delivery of HexA and B to affected neurons.

Unmet Medical Need

Tay-Sachs and Sandhoff disease are characterized by an accumulation of GM2-gangliosides due to a defective β-N-acetlyhexosaminidase protein leading to progressive, fatal neurodegeneration. There is no cure or corrective therapy for TS or SD and supportive care only marginally prolongs patient lives.

Project Objective

Our objective is to have a pre-IND meeting.

Major Proposed Activities

- Evaluate the in vitro safety and efficacy of HexA/HexB lentivector transduced human CD34+ HPC.
- Evaluate the safety of HexA/HexB lentivector transduced hematopoietic stem cells for engraftment, multi-lineage hematopoiesis, and tumorigenicity.
- Evaluate the efficacy of HexA/B lentivivector transduced hematopoietic stem cells to decrease GM2 levels, increase motor function, and prolong lives.

Statement of Benefit to California:

Tay-Sachs (TS) and Sandhoff disease (SD) are classified as rare and orphan diseases that affect patients as infants, juveniles, and adults. Currently there is no cure or effective treatment for TS or SD and supportive care can only marginally prolong the lives of patients. Our therapy would halt the progression of these diseases and after demonstrating success, would open the door for the use of hematopoietic stem cell gene therapy for the treatment of other lysosomal storage diseases.
